REMARKS

In accordance with the present invention, there are provided genes encoding neuronal nicotinic acetylcholine receptor subunits and proteins encoded thereby. In particular, the invention relates to a family of novel mammalian neuronal nicotinic acetylcholine receptor subunits. The receptor proteins are comprised of agonist binding subunits and non-agonist subunits. Agonist binding subunits of the invention include alpha2 and alpha4; non-agonist subunits include beta2, beta3 and beta4. As a result of the restriction requirement dated June 28, 2001 (Paper No. 3), and the claim amendments presented herein, the claims of the application are presently directed to beta2 subunits.

By the present communication, claims 5-9, 11, 12 and 14-16 have been amended, and new claims 18-33 have been added, in order to define Applicants' invention with greater particularity. No new matter is introduced by these amendments as they are fully supported by the specification and original claims. For the Examiner's convenience, Appendix A presents each of the amended claims reflecting the amendment thereto, and a clean copy of all the pending claims is presented herewith in Appendix B.

Drawings

In section (2) of the Action (p. 2, ll. 2-8), the drawings were objected to for reasons set forth in PTO-948, attached to the Action. Appropriate drawings are being submitted under separate cover. Reconsideration and withdrawal of the objection is respectfully requested.

Restriction; Objections to Claims 5-9, 11, 12, and 14-17

In the Office Action dated June 28, 2001 (Paper No. 3), the Examiner asserted that restriction to one of 5 groups of inventions was required, basing the assertion on the position that the claims comprise improper Markush groups. Applicants respectfully disagree with the Examiner's assertion that original claims 5-9, 11, 12, and 14-17 recite an improper Markush group (Section 3, p. 2, ll. 9-15 of the Action), for reasons set forth in the Response dated July 30,

2001. Nevertheless, in order to reduce the issues and advance prosecution, the claims have been amended herein to refer specifically to beta2 subunits only without prejudice to the claims drawn to other subunits. The claims objected to have thus been amended so as to not comprise Markush groups. Accordingly, reconsideration and withdrawal of the objection to the claims for allegedly reciting an improper Markush group is respectfully requested.

Objections to Claims 11, 12 and 16

Applicants respectfully disagree with the Examiner's assertion that claims 11, 12 and 16 are "of improper dependent form" (Section 5, p. 3, ll. 6-7 of the Action).

Nevertheless, in order to reduce the issues and advance prosecution of the application, claims 11, 12 and 16 have been amended herein so as to now be presented in independent form, consistent with the Examiner's suggestion that such amendments would obviate the objection to the claims (p. 3, ll. 8 to 9 of the Action). Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Rejections Under 35 U.S.C. §112, First Paragraph (Written Description)

The rejection of claims 5, 8, 9 and 11-17 under 35 U.S.C. §112, first paragraph as allegedly being drawn to subject matter lacking adequate written description (section 6, p. 3, ll. 18-21 of the Action) is respectfully traversed. Contrary to the Examiner's assertion, the claims are drawn to subject matter that meets the written description requirement.

Applicants respectfully disagree with the Examiner's assertion that "the instant specification does not provide a structural formula which is definitive of all proteins which might be encompassed by the term 'neuronal nicotonic acetylcholine receptor beta2 subunit'" (p. 4, l. 24 to p. 5, l. 1 of the Action). Applicants further disagree with the Examiner's assertion that the specification "does not provide a written description of a nucleic acid which can hybridize to that single disclosed nucleic acid or which has 'substantial sequence homology' thereto" (p. 5, ll. 1-3).

Contrary to the implications of the above-quoted assertions by the Examiner, the written description requirement does not require that a structure be named; rather, a structure is but one way by which the written description requirement can be met. As acknowledged by the Examiner, citing Fiers v. Revel, a written description "requires a precise definition, such as by structure, formula, chemical names or physical properties (p. 4, ll. 15-16 of the Action; emphasis added). That is, a compound can be claimed in a variety of ways, e.g., in terms of its physical properties and/or its structure, formula or chemical name.

Applicants' specification provides substantial written description of biochemical features and activities of beta2 subunits of nicotinic receptors. Specifically, beta2 subunits have amino acid residues corresponding to Cys-128 and Cys-142 of the Torpedo electric organ alpha subunit, but lack the corresponding Cys-192 and Cys-193 residues (p. 54, ll. 20-29); are refractory to being labeled by 4-(N-maleimido)benzyltrimethyl-ammoniumiodide (MBTA) (p. 62, ll. 19-23); are able to substitute for the muscle beta1 subunit in the formation of an acetylcholine receptor (p. 22, ll. 13-15 of the application), but are unable to substitute for the gamma or delta subunit of a neuronal nicotinic acetylcholine receptor (p. 58, ll. 10-12); have approximately 50% sequence identity to neuronal nicotinic acetylcholine receptor alpha subunits, (p. 53, ll. 25-27; sentence bridging pages 78 and 79; and Table 8, p. 123); are non-agonist binding subunits that do not bind acetylcholine, nicotine or analogs thereof (p. 12, ll. 4-13); form, in conjunction with an alpha3 or an alpha4 subunit, a neuronal nicotinic acetylcholine receptor that is blocked by bungarotoxin 3.1 but not by α-bungarotoxin (p. 26, ll. 3-10); and form, in conjunction with an alpha2 subunit, a neuronal nicotinic acetylcholine receptor that is not blocked by either bungarotoxin 3.1 or α-bungarotoxin (p. 26, ll. 11-15).

In view of the substantial disclosure of numerous physical and functional properties of invention beta2 subunits of neuronal nicotinic acetylcholine receptors, it is respectfully submitted that the written description requirement has been fully satisfied. A recitation of all of the sequences encompassed by the claims is not required because the claimed nucleic acids and the polypeptides encoded thereby are described in ways that do not, and need not, include specific

sequences. Accordingly, reconsideration and withdrawal f the rejection of the claims under the second paragraph of 35 U.S.C. §112, first paragraph, is respectfully requested.

Rejections Under 35 U.S.C. §112, Second Paragraph (Indefiniteness)

The rejection of claims 5-9, 11, 12 and 14-17 under 35 U.S.C. §112, second paragraph as allegedly being indefinite (sections 7-11, p. 5, l. 7 to p. 6, l. 7 of the Action) is respectfully traversed. Contrary to the Examiner's assertion, the claims clearly describe Applicants' invention. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 5-9, 11, 12 and 14-17 Under §112, 2nd Paragraph

With respect to claims 5-9, 11, 12 and 14-17 (section 7, p. 5, ll. 10-17 of the Action), Applicants respectfully disagree with the Examiner's assertion that the term "beta2 subunit" is indefinite "because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a 'beta2' subunit."

Contrary to the Examiner's assertion, Applicants' specification does identify properties that are definitive of a beta2 subunit. By way of non-limiting example, Applicants' specification discloses that beta2 subunits have amino acid residues corresponding to Cys-128 and Cys-142 of the Torpedo electric organ alpha subunit, but lack the corresponding Cys-192 and Cys-193 residues (p. 54, ll. 20-29); are refractory to being labeled by 4-(N-maleimido)benzyltrimethyl-ammoniumiodide (MBTA) (p. 62, ll. 19-23); are able to substitute for the muscle beta1 subunit in the formation of an acetylcholine receptor (p. 22, ll. 13-15 of the application), but are unable to substitute for the gamma or delta subunit of a neuronal nicotinic acetylcholine receptor (p. 58, ll. 10-12); have approximately 50% sequence identity to alpha3 and alpha4 neuronal nicotinic acetylcholine receptor subunits, (p. 53, ll. 25-27; sentence bridging pages 78 and 79; and Table 8, p. 123); are non-agonist binding subunits that do not bind acetylcholine, nicotine or analogs thereof (p. 12, ll. 4-13); form, in conjunction with an alpha3 or an alpha4 subunit, a neuronal nicotinic acetylcholine receptor that is blocked by bungarotoxin 3.1 but not by α-bungarotoxin (p.

26, ll. 3-10); and form, in conjunction with an alpha2 subunit, a neuronal nicotinic acetylcholine receptor that is not blocked by either bungarotoxin 3.1 or α-bungarotoxin (p. 26, ll. 11-15).

Applicants' specification notes that some description of beta2 subunits has been published as: Deneris et al., Primary Structure and Expression of Beta 2: A Novel Subunit of Neuronal Nicotinic Acetylcholine Receptors. Neurons 1:45-54, 1988 (p. 6, ll. 18-24, of the application). Since the publication of Deneris et al. article in 1988, workers in the field of molecular biology have continued to use the term "beta2 subunit" without any apparent confusion. See, for example, Corringer et al., Nicotinic Receptors at the Amino Acid Level. Annu. Rev. Pharmacol. Toxicol. 40:31-458, 2000 (copy attached for the Examiner's convenience). Thus, workers in the field of molecular biology have used the phrase "beta2 subunit" for over a decade and clearly do not find the term indefinite. Accordingly, Applicants' use of the term "beta2 subunit" is respectfully submitted to be clear.

Rejection of Claims 8 and 9 Under §112, 2nd Paragraph

Applicants respectfully disagree with the Examiner's assertion that claims 8 and 9 are allegedly vague and indefinite because they recite the limitation "functionally equivalent" without identifying those functions whose presence are being required. Contrary to the Examiner's assertion, the claims need not be limited to a list of specific activities and/or characteristics in order to be clear.

Claims 8 and 9 have been amended by way of the present communication so as to not recite a "functionally equivalent" DNA. Rather, in the claims as amended, it is the beta2 subunit encoded by the claimed DNA that is functionally equivalent to the beta2 subunit of pPCX49, ATCC No. 67643 (claim 8), or to the beta2 subunit shown in Figure 7B(1), 7B(2) and 7B(3) (claim 9). It is respectfully submitted that the claims are not indefinite when viewed in the appropriate context.

It is axiomatic that the claims of a patent are interpreted not in isolation, but rather in the context of the patent application. "Claims must be read in view of the specification." *Markman*

v. Westview Instruments, Inc., 52 F.3d 967, 34 U.S.P.Q.2d 1321 (Fed. Cir. *en banc* 1995); *aff'd*, 116 S. Ct. 1384 (1996). It is believed that Applicants' disclosure provides adequate disclosure for assessing the functional equivalence of a beta2 subunit based on the numerous physical and functional properties thereof that are discussed in the preceding sections. One skilled in the art would be able to determine which of these properties, and/or later-discovered properties of beta2 polypeptides, is appropriate to identify "functionally equivalent" sequences in any given context. Thus, the claims need not be limited to a list of specific properties, because one skilled in the art will be able to identify a beta2 subunit in a given set of circumstances using any of the attributes of beta2 subunits described in Applicants' specification.

Rejection of Claim 11 Under §112, 2nd Paragraph

Applicants respectfully disagree with the Examiner's assertion that claim 11 is allegedly indefinite "because the metes and bounds of the limitation 'having substantial sequence homology' are undeterminable" (section 9, page 5, last two lines). Contrary to the Examiner's assertion, the metes and bounds of the claims are clear to one skilled in the art in view of Applicants' disclosure.

By way of the present communication, claim 11 has been amended so that the beta2 subunit claimed thereby "has greater than 68% sequence identity with the beta2 subunit shown in Figures 7B(1), 7B(2), and 7B(3)." Applicants specification clearly describes sequence identity and provides several examples thereof.

For example, the specification discloses that:

> Protein sequences were aligned using an INTELLIGENETICS software IFIND program that utilizes an algorithm developed by Wilbur and Lipman (1983)*. Parameters were set to default values. Alignments were adjusted by visual inspection. Homology percentages were calculated by dividing the number of identical residues by the number of residues in the shorter of the two sequences being compared.

P. 47, ll. 5-12 of the application. (*The complete citation for "Wilbur and Lipman (1983)" is Wilbur, W. J., and Lipman, D. J. (1983). Rapid similarity searches of nucleic acid and protein data banks. Proc. Natl. Acad. Sci., USA 80, 726-730. See p. 146, ll. 28-30 of the application.)

The specification provides several examples of the application of the above teachings to determine the % sequence identity between two or more sequences, for example:

> The mature alpha2 protein has 49, 57 and 67% amino acid sequence identity with the mature alpha1, alpha3 and alpha4 proteins, respectively. The percentages of sequence identity were calculated by dividing the number of identical residues by the number of residues in the shorter of the two compared sequences.

P. 24, ll. 24-30 of the application.

> Deduced amino acid sequences were aligned and the percent sequence identity calculated by dividing the number of identical residues by the number of residues in the shorter of two subunits being compared.

P. 68, ll. 26-30 of the application.

The specification also provides exemplary alignments of various sets of sequences of neuronal nicotinic acetylcholine receptor subunits. See, e.g., Figures 3(A), 3(B), 8, 11, 16, 20, 26 and 27.

In view of the extensive guidance provided by Applicants' specification, it is respectfully submitted that one skilled in the art could readily apply the teachings of Applicants' disclosure to determine whether or not a protein has an amino acid sequence that falls within a given range of % sequence identity. Accordingly, the metes and bounds of claim 11 are respectfully submitted to be clear to those skilled in the art.

Rejection of Claims 15, 25 and 26 Under §112, 2nd Paragraph

Applicants respectfully disagree with the Examiner's assertion that claim 15 is allegedly indefinite "because the limitation 'under stringent conditions' is conditional and no specific conditions are recited in either the claims or the specification." Contrary to the Examiner's assertion, the phrase "under stringent conditions" is clear to one skilled in the art.

It is respectfully submitted that a skilled artisan readily understands the meaning of the phrase "under stringent conditions" as used in the context of "hybridizes under stringent conditions." As noted in Applicants' disclosure, hybridization methods are well known to those skilled in the art of molecular biology (p. 24, ll. 15-20). In the specification, exemplary teachings of hybridization are stated to be found in Nef, P., Oneyser, C., Barkas, T., and Ballivet, M. (1986). Acetylcholine receptor related genes expressed in the nervous system. In Nicotinic Acetylcholine Receptor: Structure and Function. A Maelicke, ed., Springer-Verlag, pp. 417-422; and Benton, W. and Davis, R. (1977). Science 196, 180-182 (p. 24, ll. 15-18).

In addition, the specification provides exemplary "hybridization procedures and conditions in the va[r]ious experimental sections of this specification" (p. 24, ll. 18-20). Applicants' disclosure provides examples of hybridization conditions that are stringent for the described application. For example, in the section describing the preparation and screening of cDNA libraries, the disclosure explains how

> Total RNA was obtained as previously described (Goldman, et al., 1987) or by the method of Cathala, et al., (1983). Poly(A)+ RNA was selected using an oligo-dT cellulose column (Aviv and Leder, 1972). The cDNA was synthesized by the method of Gubler and Hoffman (1983) from poly(A)+ RNA that was obtained from a rat hypothalamic punch and PC12 cells. The cDNA was ligated to phosphorylated EcoRI linkers and cloned into the EcoRI site of bacteriophage λ gt10 (Huynn, et al., 1985). Approximately 5 times 10^5 recombinants from the hypothalamus library and 1 times 10^6 recombinants from the PC12 library were screened with a [^{32}P]-nick-translated PCA48 cDNA (Boulter, et al., 1986) or 15-1 insert, respectively. Filter hybridization was performed overnight in 5X

> SSPE, 1% SDS, 1X Denhardt's at 65°C. Filters were washed twice at room temperature for 30 min in 2X SSC and once at 65°C for 1 hr in 0.2X SSC and 1% SDS.

P. 68, ll. 3-20 of the application.

In each hybridization, a few clones were identified that hybridized to a radiolabeled probe under the conditions. Specifically,

> Screening 5 times 10^5 recombinants resulted in the isolation of clones, 15-1 (1324 bp), 122-1 (1834 bp), and 133-1 (1706 bp) (FIG. 7A), encoding a protein related to, but different from, the alpha2, alpha3 and alpha4 subunits * * * Screening 1 times 10^6 recombinants with a probe made from clone 15-1 resulted in the isolation of several clones, one of which, 1PCX49 (2196 bp), was chosen for further study (FIG. 7A).

P. 52, l. 19 to p. 53, l. 1 of the application.

Thus, the above-described conditions are sufficiently stringent for the purpose of screening 10^5 to 10^6 clones in order to identify a few clones that hybridize to the above-described probe DNA.

Based on the well known meaning of "stringent" to those in the field of the invention, taken with the exemplary teachings of Applicants' disclosure, the term "under stringent conditions" as consistently used throughout Applicants' specification and claims, is respectfully submitted to be clear to those skilled in the art. Accordingly, Applicants' use of the term "under stringent conditions" is respectfully submitted to be clear.

Rejection of Claim 16 Under §112, 2nd Paragraph

Pursuant to the Examiner's observation that there was no antecedent basis in original claim 16 for the phrase "the nucleic acid of claim 7," this issue has been obviated by amendment of claim 16 to be independent rather than dependent on claim 7. Accordingly, no antecedent basis is needed for the phrase "the nucleic acid of claim 7" because that term is no longer used in claim 16.

Summary of Response to the Rejection of Claims Under §112, 2nd Paragraph

It is respectfully submitted that the pending claims are not indefinite to one skilled in the art. Reconsideration and withdrawal of the rejection of claims under the second paragraph of 35 U.S.C. §112 as allegedly being indefinite are thus respectfully requested.

Rejections Under 35 U.S.C. §101 (Non-Statutory Subject Matter)

The rejection of claims 7-9, 11, 12 and 16 under 35 U.S.C. §101 as allegedly being drawn to non-statutory subject matter (sections 12 and 13; p. 6, ll. 8-18 of the Action) is respectfully traversed. Contrary to the Examiner's assertion, the claims are drawn to statutory subject matter.

By the present communication, the claims have been amended so that neither DNA sequences nor products of nature are encompassed by the claims. It is respectfully submitted that the amendments to the claims presented herein obviate the rejections under 35 U.S.C. §101.

Specifically, claims 7-9, 12 and 16, as amended herein are drawn to, e.g., a "DNA having nucleotide sequences" as opposed to a "DNA sequence." The amended claims are thus clearly drawn to DNA molecules per se, and such molecules are statutory subject matter.

Claims 11, 12 and 16, as amended herein, include the term "substantially pure" clearly rendering the claimed molecules statutory subject matter as RNA does not occur in a substantially purified state in nature.

It is respectfully submitted that the amendments to the claims presented herein make it clear that the claims encompass statutory subject matter. Reconsideration and withdrawal of the rejection under 35 U.S.C. §101 are thus respectfully requested.

Conclusion

In view of the above amendments and remarks, the present application is respectfully submitted to be in condition for allowance. Accordingly, reconsideration and favorable action with respect to the pending claims are respectfully requested. In the event any issues remain to be resolved in view of this communication, the Examiner is invited to contact the undersigned at the number given below.

Respectfully submitted,

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Enclosures: Appendix A, Version With Markings to Show Changes Made
Appendix B, Pending Claims
Corringer *et al.*, Nicotinic Receptors at the Amino Acid Level. *Annu. Rev. Pharmacol. Toxicol. 40*:31-458, 2000

APPENDIX A

Versi n With Markings to Show Changes Made

5. (Amended) A substantially pure **[double-stranded]** DNA wherein the sense strand of said DNA encodes the primary amino acid sequence of a beta2 subunit of a neuronal nicotinic acetylcholine receptor **[polypeptide selected from the group consisting of alpha2, alpha4, beta2, and beta3]**.

6. (Amended) **[A]** The substantially pure **[double-stranded]** DNA of claim 5 wherein said **[alpha subunit(s) are encoded by DNA sequences selected from the group consisting of pHYP16, ATCC No. 67646, which encodes alpha2; pPCA48, ATCC No. 67642, which encodes alpha3; pHYA23-l(E)1, ATCC No. 67644, which encodes alpha4.1; and pHIP3C(E)3, ATCC No. 7645, which encodes alpha4.2; and said beta subunit(s) are encoded by DNA sequences selected from the group consisting of]** DNA is the protein coding region of pPCX49, ATCC No. 67643**[, which encodes beta2; and ESD76, ATCC No. 67653, which encodes beta 3]**.

7. (Amended) Substantially pure DNA having the protein coding region of the nucleotide sequence**[s selected from the group consisting of DNA sequences]** shown in **[Figures 2A(1), 2(A(2), 2A(3) (for alpha4.1); Figures 2B(l), 2B(2), 2B(3) (for alpha4.2);]** Figures 7B(1), 7B(2), and 7B(3) **[(for beta2); Figures 15C(1), 15C(2), 15C(3) (for alpha2); and Figure 19 (for Beta3)]**.

8. (Amended) Substantially pure DNA having a nucleotide sequence**[s]** that **[are]** encodes a beta2 subunit of a neuronal nicotinic acetylcholine receptor, wherein said beta2 subunit is functionally equivalent to **[any of the substantially pure DNA sequences selected from the group c nsisting of: pHYP16, ATCC N . 67646, which enc des alpha2; pHYA23-1, ATCC No. 67644, which encodes alpha4.1; pHIP3C(E)3, ATCC No. 67645, which encodes**

alpha4.2;] the beta2 subunit encoded by the protein coding region of pPCX49, ATCC No. 67643**[, which encodes beta2 ESD76, ATCC No. 67653, which encodes beta3]**.

9. (Amended) Substantially pure DNA having a nucleotide sequence**[s]** that **[are]** encodes a beta2 subunit of a neuronal nicotinic acetylcholine receptor, wherein said beta2 is functionally equivalent to **[any of the substantially pure DNA sequences]** the beta2 subunit shown in **[Figures 2A(1), 2(A(2), 2A(3) (for alpha4.l); Figures 2B(1), 2B(2), 2B(3) (for alpha4.2);]** Figures 7B(1), 7B(2), and 7B(3) **[(for beta2); Figures 15C(1), 15C(2), 15C(3) (for alpha2); and Figure 19 (for Beta3)]**.

[10. (not elected)]

11. (Amended) Substantially pure DNA **[having substantial sequence homology with the DNA of Claim 5]** encoding a beta2 subunit of a neuronal nicotinic acetylcholine receptor, wherein the amino acid sequence of said beta2 subunit has greater than about 68% sequence homology with the beta2 subunit shown in Figures 7B(1), 7B(2), and 7B(3).

12. A substantially pure mRNA having a nucleotide sequence**[s]** transcribed from **[the substantially pure]** DNA **[of Claim 5]** wherein the sense strand of said DNA encodes the primary amino acid sequence of a beta subunit of a neuronal nicotinic acetylcholine receptor.

[13. (not elected)]

14. Cells transformed by the substantially pure DNA of Claim 5.

15. Isolated nucleic acid that hybridizes under stringent conditions to nucleic acid having a nucleotide sequence**[s]** encoding **[polypeptides selected from]** the polypeptide sequence**[s]** set forth in **[Figures 15C(1-3) (for alpha 2); Figures 2A(l-3) (for alpha4.1);**

Figures 2B(1-3) (for alpha4.2);] Figures **[7B(1-2) (for beta2); and Figure 19 (for beta3)]** 7B(1), 7B(2), and 7B(3).

16. A substantially pure RNA having a nucleotide sequence that is complementary to the **[nucleic acid]** DNA of claim [7] 5.

APPENDIX B

Pending Claims

5. A substantially pure DNA wherein the sense strand of said DNA encodes the primary amino acid sequence of a beta2 subunit of a neuronal nicotinic acetylcholine receptor.

6. The substantially pure DNA of claim 5 wherein said DNA is the protein coding region of pPCX49, ATCC No. 67643.

7. Substantially pure DNA having the protein coding region of the nucleotide sequence shown in Figures 7B(1), 7B(2), and 7B(3).

8. Substantially pure DNA having a nucleotide sequence that encodes a beta2 subunit of a neuronal nicotinic acetylcholine receptor, wherein said beta2 subunit is functionally equivalent to the beta2 subunit encoded by the protein coding region of pPCX49, ATCC No. 67643.

9. Substantially pure DNA having a nucleotide sequence that encodes a beta2 subunit of a neuronal nicotinic acetylcholine receptor, wherein said beta2 subunit is functionally equivalent to the beta2 subunit encoded by the nucleotide sequence shown in Figures 7B(1), 7B(2), and 7B(3).

11. Substantially pure DNA encoding a beta2 subunit of a neuronal nicotinic acetylcholine receptor, wherein the amino acid sequence of said beta2 subunit has greater than 68% sequence identity with the beta2 subunit shown in Figures 7B(1), 7B(2), and 7B(3).

12. A substantially pure mRNA having a nucleotide sequence transcribed from DNA, wherein the sense strand of said DNA encodes the primary amino acid sequence of a beta2 subunit of a neuronal nicotinic acetylcholine receptor.

14. Cells transformed by the substantially pure DNA of Claim 5.

15. Isolated nucleic acid that hybridizes under stringent conditions to nucleic acid having a nucleotide sequence encoding the polypeptide sequence set forth in Figures 7B(1), 7B(2), and 7B(3).

16. A substantially pure RNA having a nucleotide sequence that is complementary to the nucleotide sequence of the DNA of claim 5.

17. A vector containing the nucleic acid of claim 5.

18. A substantially pure DNA wherein the sense strand encodes the amino acid sequence of a beta2 subunit of a neuronal nicotinic acetylcholine receptor, wherein said beta2 subunit has the ability to substitute for the muscle beta1 subunit in the formation of an acetylcholine receptor, and wherein said beta2 subunit is not able to substitute for the gamma or delta subunit of a neuronal nicotinic acetylcholine receptor.

19. The substantially pure DNA of claim 18, wherein a neuronal nicotinic acetylcholine receptor comprising said beta2 subunit and an alpha2 subunit is not blocked by either bungarotoxin 3.1 or α-bungarotoxin.

20. The substantially pure DNA of claim 18, wherein said beta2 subunit forms, with an alpha3 or an alpha4 subunit, a neuronal nicotinic acetylcholine receptor that is blocked by bungarotoxin 3.1 but not by α-bungarotoxin.

21. The substantially pure DNA of claim 18, wherein said beta2 subunit has amino acid residues corresponding to Cys-128 and Cys-142 of the Torpedo electric organ alpha subunit, but lacking the corresponding Cys-192 and Cys-193 residues.

22. The substantially pure DNA of claim 18, wherein said beta2 subunit has approximately 50% sequence identity to neuronal nicotinic acetylcholine receptor alpha subunits.

23. The substantially pure DNA of claim 18, wherein said beta2 subunit is not labeled by 4-(N-maleimido)benzyltrimethyl-ammoniumiodide (MBTA).

24. A substantially pure DNA wherein the sense strand encodes the amino acid sequence of a beta2 subunit of a neuronal nicotinic acetylcholine receptor, wherein said beta2 subunit has two or more properties selected from the group consisting of:

(a) being able to substitute for the muscle beta1 subunit in the formation of an acetylcholine receptor;

(b) not being able to substitute for the gamma or delta subunit of a neuronal nicotinic acetylcholine receptor;

(c) not being labeled by 4-(N-maleimido)benzyltrimethyl-ammoniumiodide (MBTA);

(d) having amino acid residues corresponding to Cys-128 and Cys-142 of the Torpedo electric organ alpha subunit, but lacking the corresponding Cys-192 and Cys-193 residues;

(e) having approximately 50% sequence identity to neuronal nicotinic acetylcholine receptor alpha subunits;

(f) not binding acetylcholine, nicotine or analogs thereof;

(g) forming, in conjunction with an alpha3 or an alpha4 subunit, a neuronal nicotinic acetylcholine receptor that is blocked by bungarotoxin 3.1 but not by α-bungarotoxin; and

(h) forming, in conjunction with an alpha2 subunit, a neuronal nicotinic acetylcholine receptor that is not blocked by either bungarotoxin 3.1 or α-bungarotoxin.

25. Isolated nucleic acid that hybridizes under stringent conditions to the cloned EcoRI fragment insert in pPCX49, ATCC No. 67643.

26. A substantially pure nucleic acid, the sense strand of which encodes the amino acid sequence of a beta2 subunit of a neuronal nicotinic acetylcholine receptor, wherein said nucleic acid hybridizes under stringent conditions to a radiolabeled probe made from a cloned cDNA encoding an alpha3 subunit of a neuronal nicotinic acetylcholine receptor.

27. The substantially pure nucleic acid of claim 26, wherein said cloned cDNA encoding an alpha3 subunit of a neuronal nicotinic acetylcholine receptor is the cloned DNA insert in pPCA48, ATCC No. 67642.

28. A substantially pure and/or synthetic nucleic acid probe for detecting nucleic acids encoding a beta2 subunit of a neuronal nicotinic acetylcholine receptor, said nucleic acid probe comprising a set of contiguous nucleotides, said probe having a sequence of at least about 15 contiguous nucleotides derived from the nucleotide sequence of the DNA of claim 5.

29. A substantially pure and/or synthetic nucleic acid probe for detecting nucleic acids encoding members of the neuronal nicotinic acetylcholine receptor gene family, said probe having a sequence of at least about 15 contiguous nucleotides derived from a sequence that encodes a transmembrane domain selected from the group consisting of TMD I, TMD II, TMD III and TMD IV of the beta2 neuronal nicotinic acetylcholine receptor subunit polypeptide shown in Figure 8.

30. A substantially pure and/or synthetic nucleic acid probe for detecting nucleic acids encoding beta2 subunit of a neuronal nicotinic acetylcholine receptor, said probe having a sequence of at least about 15 contiguous nucleotides from a sequence that encodes the cytoplasmic domain of the beta2 subunit shown in Figure 8.

31. Cells transformed by the substantially pure DNA of Claim 24.

32. A vector containing the nucleic acid of claim 24.

33. Substantially pure DNA having the nucleotide sequence of residues –179 to –1 in Figures 7B(1) or residues 1510-2017 of Figure 7B(3).